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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,701	12/11/2006	Karin Ekberg	CBX0007-506-US	3695

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GLOBAL PATENT GROUP - CBX
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EXAMINER

MACFARLANE, STACEY NEE

ART UNIT	PAPER NUMBER
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1649

NOTIFICATION DATE	DELIVERY MODE
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03/30/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/575,701	Applicant(s) EKBERG ET AL.	
	Examiner STACEY MACFARLANE	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3 and 10-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 13 is/are allowed.
- 6) ☒ Claim(s) 3, 10-12, 14 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/11/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 3 and 15 have been amended as requested in the amendment filed on February 11, 2010. Following the amendment, claims 3 and 10-15 are pending in the instant application and are under examination in the instant office action.
2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
3. Applicant's arguments filed on February 11, 2010 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. As currently amended, Claims 3, 10, 12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Fernqvist-Forbes et al., Metabolic and Pharmacokinetic Responses to Subcutaneous Injection of Combined C-Peptide and Insulin in Type 1 Diabetes, Diabetologia, 36 (Suppl 1): A1-222, 1993, Abstract 483 on page A126.

Claims 3, 10, 12 and 14 are drawn to a method of treating diabetes and/or diabetes-related microvascular complications comprising administering C-peptide or a pharmaceutical composition comprising C-peptide to a patient once daily, wherein said once daily administration does not include continuous administration of the presence of rate-controlling agents and said administration is subcutaneous (claim 3); wherein the C-peptide is human (claim 10); the patient is human (claim 12); and the C-peptide is in an aqueous solution (claim 14).

As previously noted, there is no explicit definition provided for the “rate-controlling agents” of the claims, nor is there explicit guidance as to what constitutes “continuous administration” or “prolonged period of time”. Absent specific guidance within the disclosure, the claim is interpreted as encompassing a once daily administration, by any mode other than osmotic pump and excluding infusions that go beyond the bounds of 24 hours (“daily” of the claims). Claim language is open ended (“comprising”) thus the method of the claim comprises administration of at least C-peptide but does not specifically exclude the administration of other agents in combination with said C-peptide.

The Fernqvist-Forbes et al. reference discloses a method comprising administering a single subcutaneous administration of 60 nmol/L of biosynthetic human c-peptide to Type 1 diabetic human patients in a saline solution. Thus, the method of the invention fails to distinguish over that within the prior art disclosure.

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6. As currently amended, Claims 3, 10, 12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Linde B., Absorption of C-peptide after subcutaneous injection in type 1 diabetic patients, In: "C-Peptide and type 1 diabetes mellitus", An International Symposium, Karolinska Institute, Stockholm Sweden, September 23-24, 1994.

Claims 3, 10, 12 and 14 are drawn to a method of treating diabetes and/or diabetes-related microvascular complications comprising administering C-peptide or a pharmaceutical composition comprising C-peptide to a patient once daily, wherein said once daily administration does not include continuous administration of the presence of rate-controlling agents and said administration is subcutaneous (claim 3); wherein the C-peptide is human (claim 10); the patient is human (claim 12); and the C-peptide is in an aqueous solution (claim 14).

As previously noted, there is no explicit definition provided for the "rate-controlling agents" of the claims, nor is there explicit guidance as to what constitutes "continuous administration" or "prolonged period of time". Absent specific guidance within the disclosure, the claim is interpreted as encompassing a once daily administration, by any mode other than osmotic pump and excluding infusions that go beyond the bounds of 24 hours ("daily" of the claims). Claim language is open ended ("comprising") thus the method of the claim comprises administration of at least C-peptide but does not specifically exclude the administration of other agents in combination with said C-peptide.

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The Linde reference discloses a method comprising administering a single subcutaneous administration of 60 nmol/L of biosynthetic human c-peptide to Type 1 diabetic human patients in a saline solution. Thus, the method of the invention fails to distinguish over that within the prior art disclosure.

7. As currently amended, Claims 3, 10, 12 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wahren et al., Journal of Internal Medicine, 240: 115-124, 1996 cited as reference 5, on the IDS filed February 11, 2010.

Claims 3, 10 and 12-15 are drawn to a method of treating diabetes and/or diabetes-related microvascular complications comprising administering C-peptide or a pharmaceutical composition comprising C-peptide to a patient once daily, wherein said once daily administration does not include continuous administration of the presence of rate-controlling agents and said administration is subcutaneous (claim 3); wherein the C-peptide is human (claim 10); the patient is human (claim 12) and the C-peptide is in an aqueous solution (claim 14); and the complications are neuropathy.

The Wahren et al. prior art teaches a single subcutaneous administration of 60 nmol of c-peptide to human insulin-dependent diabetes mellitus patients (Figure 6, page 121 and page 122, last paragraph). Additionally, the Wahren et al reference teaches C-peptide as a therapeutic treatment for diabetic neuropathy (pages 117-118). Specifically, the reference states: "A beneficial effect of C-peptide on nerve function in IDDM patients during both short- and long-term administration" (page 118, column 2,

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first paragraph). Thus, the method of the invention fails to distinguish over that disclosed within the prior art.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. As currently amended, Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fernqvist-Forbes et al. (1993) as applied to claims 3, 10 and 12-14 above, and further in view of Wahren et al., (1998) cited in the previous Office action.

The Fernqvist-Forbes et al. reference discloses a method comprising administering human recombinant C-peptide at 60 nmol/L to type 1 diabetic patients.

The Fernqvist-Forbes et al. reference does not teach administration wherein the C-peptide is the fragment EGSLQ (SEQ ID NO: 2), as required by instant claim 11. The Wahren et al. reference, however, teaches that the fragment consisting of SEQ ID NO:

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2 (which is identical to SEQ ID NO: 3 or "Peptide E" of Wahren reference) has the same stimulatory activity and molecular effect as full-length C-peptide (Example 1).

In *KSR International Co. v. Teleflex, Inc.*, the Supreme Court has stated that combining prior art elements according to known method to yield predictable results is *prima facie* obvious if the following rationale can be applied:

- (1) the prior art includes each element claimed though not necessarily in the same reference.
- (2) it was within the technical grasp of one of ordinary skill in the art to combine the elements as claimed by known methods, and that in combination, each element merely would have performed the same function as it did separately.
- (3) one of ordinary skill in the art would have recognized that the results of such combination were predictable.

(*KSR International Co. v. Teleflex, Inc.* 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007).

One of ordinary skill in the art would recognize the use of the EGSLQ pentapeptide fragment, equivalent to claimed SEQ ID NO: 2, taught by Wahren et al. in the method of Fernqvist-Forbes et al. A skilled artisan would be motivated to combine the prior art elements because this specific fragment maintains the stimulatory activity and thus would result in the predictable effect of treating diabetic renal nephropathy. Based upon the guidance and direction within the prior art, such combination would have been well within the technical grasp of a skilled artisan. Since each of the elements in combination are merely performing the same function as they did separately, then one of ordinary skill in the art would have been able to predictably combine the elements with a reasonable expectation of success. Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

Conclusion

11. Claim 13 appears to be free of the prior art and would be allowable if written in independent form.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **STACEY MACFARLANE** whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649